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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/822,295	04/02/2001	Bahija Jallal	038602/1125	8862

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EXAMINER	
HOLLERAN, ANNE L	

ART UNIT	PAPER NUMBER
1642	10

DATE MAILED: 10/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/822,295	JALLAL ET AL.
	Examiner	Art Unit
	Anne Holleran	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 10-12 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 10-12 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8,9 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The preliminary amendment filed Feb. 7, 2002 is acknowledged. Claims 1-9 and 13-22 were canceled. Claims 10-12 are pending and examined on the merits.

Claim Rejections - 35 USC § 112

2. Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 is indefinite because it is drawn to polypeptides that lack one or more fragments of SEQ ID NO: 2. This may result in a structure that lacks all of the amino acids of SEQ ID NO: 2. Thus, claim 12 is drawn to polypeptides for which there is no structural description.

3. Claims 10-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polypeptides that comprise the amino acid sequence set forth in SEQ ID NO: 2, does not reasonably provide enablement for the full scope of the claimed genus of PTP04 polypeptides, as contemplated in the specification, page 16, line 24 to page 22, line 23, and as claimed in claims 11 and 12, where the claimed polypeptides may only comprise a fragment of SEQ ID NO: 2, or comprise a sequence that is completely unrelated to SEQ ID NO: 2. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation would be required to practice the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See Ex parte Forman, 230 USPQ 546, BPAI, 1986.

The claims are broadly drawn to isolated, enriched or purified PTP04 polypeptides, polypeptides comprising fragments of a protein encoded by the amino acid sequence of SEQ ID NO: 2, and drawn to polypeptides that lack one or more segments of the polypeptide of SEQ ID NO: 2, where the segments are defined as amino acid residues, 1-48, 49-294, 295-807, an N-terminal domain, a catalytic domain, and a C-terminal domain. Thus, the claims are drawn to a large genus of polypeptide structures, where many of the species have very little in common with the structure of the one exemplified PTP04 polypeptide, that of a polypeptide having the amino acid sequence of SEQ ID NO: 2.

The specification teaches one example of a PTP04 polypeptide, and teaches that it is defined by the primary amino acid sequence set forth in SEQ ID NO: 2. This sequence is derived from a cDNA sequence that was discovered to be differentially expressed in tumor cells relative to non-tumor cells, and is asserted to be the sequence of an intracellular tyrosine phosphate. Therefore, the specification enables the use of polypeptides comprising the full sequence of SEQ ID NO: 2, because such a sequence has enzymatic activity of a tyrosine

phosphatase, and may be used by one of skill in the art to catalyze a tyrosine phosphatase reaction. However, the specification fails to disclose any examples of variants of SEQ ID NO: 2 that could be used by one of skill in the art to catalyze a tyrosine phosphatase reaction. The description of PTP04 polypetpides that is provided in the specification amounts to a wish or hope of discovering variants that are encompassed by the claimed genus. Thus, although the specification provides a structural description of what structures are contemplated, this does not amount to an enabling disclosure for how to use the a representative number of species because it is not clear that the described variants will have the same enzymatic activity, or any activity at all, that the polypeptide comprising the amino acid sequence of SEQ ID NO: 2 has.

Furthermore, the study of the relationship between the primary amino acid sequence and protein function is highly unpredictable. Bowie et al (Science, 247: 1306-1310, 1990) teaches that while it is known that many amino acid substitutions are possible in any given protein, the position with the protein sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Burgess et al (J. Cell Biology, 111 : 2129-2138, 1990) teaches that replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Lazar et al (Molecular and Cellular Biology, 8: 1247-1252, 1988) teaches that replacement of aspartic acid at position 47 with alanine or asparagines does not affect biological activity while replacement with serine or glutamic acid sharply reduces the biological activity of the protein. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and

characteristics of a protein. Therefore, the claims are drawn to a highly variant genus of polypeptide structures, which may have widely varying biogical functions, or no function at all.

It is noted that the specification teaches that the mRNA that encodes the amino acid sequence of SEQ ID NO: 2 is differentially expressed in tumor cells. However, this teaching is not sufficient to enable one of skill in the art to use the encoded protein for diagnosis of cancer, because the relationship between cancer and the expression of the protein product is not established by the disclosure of the specification. Many other proteins are regulated at the translational level rather than the transcriptional level. For instance, Shantz and Pegg (Int J of Biochem and Cell Biol., 1999, Vol. 31, pp. 107-122) teach that ornithine decarboxylase is highly regulated in the cell at the level of translation and that translation of ornithine decarboxylase mRNA is dependent on the secondary structure of the mRNA and the availability of eIF-4E, which mediates translation initiation. McClean and Hill (Eur J of Cancer, 1993, vol. 29A, pp.2243-2248) teach that p-glycoprotein can be overexpressed in CHO cells following exposure to radiation, without any concomitant overexpression of the p-glycoprotein mRNA. In addition, Fu et al (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Thus, predictability of protein translation is not necessarily contingent on mRNA expression due to the multitude of homeostatic factors affecting transcription and translation. Thus, given the state of the art as reviewed above, the differential expression of mRNA in tumor cells cannot be used as a basis for the proposition that detection of the claimed polypeptides may be used for detection

of tumor cells, because the specification has not correlated the expression of the claimed polypeptides with the treatment or diagnosis of a disease.

Because the enablement of the one exemplified species of PTP04 is narrowly based on the ability of one of skill in the art to use the polypeptide as tyrosine phosphatase, the specification fails to enable the claims that are directed to polypeptides comprising fragments, or to polypeptides that are sequence variants of PTP04, because it is highly unpredictable whether any of these species will have the same biological activity as that of the exemplified polypeptide comprising the amino acid sequence of SEQ ID NO: 2. Therefore, in view of the broadly claimed genus, the narrow basis for the enablement of use of the exemplified polypeptide species and the unpredictable nature of protein chemistry, it would require undue experimentation for one of skill in the art to use polypeptides as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (c) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

4. Claims 10-12 are rejected under 35 U.S.C. 102(a) as being anticipated by Accession No. Q93095, Database SPTREMBL, 01 February 1997, Dayton, M.A. et al).

Claims 10-12 may be interpreted as drawn to polypeptides that comprise fragments of SEQ ID NO: 2. Accession No. Q93095 teaches a polypeptide that comprises amino acids 164-243 of SEQ ID NO: 2, thus, describing a sequence that lacks at least one of the domains listed in claim 12. Therefore, Accession No. Q93095 teaches a polypeptide that is the same as that claimed.

5. Claims 10-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Matthews et al (Matthews, R.J. et al., Mol. Cell. Biol. 12: 2396-2404, 1992; cited in the IDS).

Claims 10-12 may be interpreted as drawn to polypeptides that comprise fragments of SEQ ID NO: 2. Matthews teaches a polypeptide sequence that comprises amino acids 89-120 of SEQ ID NO: 2, thus describing a sequence that lacks at least at least one of the domains listed in claim 12. Thus, Matthews teaches a polypeptide that is the same as that claimed.

6. Claims 10-12 are rejected under 35 U.S.C. 102(e) as being anticipated by Cheng et al (U.S. 6,238,902; issued May 29, 2001; effective filing date March 20, 1997). Claims 10-12 may be interpreted as drawn to polypeptides that comprise fragments of SEQ ID NO: 2 or that have high sequence similarity with the amino acid sequence of SEQ ID NO: 2. Cheng teaches a polypeptide that comprises the fragment of SEQ ID NO: 2, amino acids 790-802, thus, describing a sequence that lacks at least one of the domains listed in claim 12. Also, Cheng teaches a polypeptide that has almost 90 percent sequence similarity over amino acids 24 to 294

of SEQ ID NO: 2. Thus, Cheng discloses a polypeptide sequence that is the same as that claimed.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892. Examiner Holleran can normally be reached Monday through Friday, 9:30 am to 2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 308-0196.

Anne L. Holleran
Patent Examiner
September 30, 2002